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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,385	07/06/2001	Joyce A. Deleo	DC-0156	4729

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
06/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	09/857,385	DELEO ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date. _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Applicants' arguments filed February 18, 2009 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim 1 is pending in this application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yaksh et al. U.S. Patent No. 5,180,716 A. and Heywood et al. and in further view of Drug Facts and Comparisons.

Yaksh et al. teach that spinal (intrathecal/epidural) administration of centrally acting agents, such as antineoplastics and analgesics is shown to have considerable therapeutic efficacy for treatment of pain, spasticity, central nervous system tumors and infections (column 1, lines 18-25) and teach that methotrexate is one of these centrally acting agents that is by intrathecal infusion (column 8, lines 33-39 and column 8, line 66 to column 9, line 8). Yaksh et al. does not teach treatment of radiculopathy, however Heywood et al. that rheumatoid arthritis causes cervical spine instability and is a causative factor in symptoms of radiculopathy (see abstract). Drug Facts and Comparisons teach administration of methotrexate for rheumatoid arthritis by ameliorating symptoms of inflammation (pain, swelling, stiffness) (page 1243).

It would have been made obvious to one of ordinary skill in art at the time it was made to employ methotrexate administered intrathecally for treatment of lower back pain with radiculopathy motivated by the teaching of Yaksh et al., who teaches the efficacy of methotrexate administered intrathecally and the teaching of the Heywood et al. that Rheumatoid arthritis causes cervical spine instability and is a causative factor in symptoms of radiculopathy (see abstract) combined with the teachings of Drug Facts and Comparisons that methotrexate is routinely employed for treatment of rheumatoid arthritis by ameliorating symptoms of inflammation.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Response to Arguments

Applicant is in disagreement with the Examiner's rejection supra and states that a key limitation in the pending claim related to the dose of the methotrexate administered intrathecally is not discussed. In response, the instant claims are drawn to an animal. When one looks that the specification for clarification of the animal, page 7 of the instant specification identifies the animal as a rat. The claim states that dosages of 1 mg/kg are to be administered, but does not state the frequency of the administration. Drug Facts and Comparisons teach administration of methotrexate at a dose of 7.5 mg/week. One having ordinary skill in the art could readily extrapolate this dosage amount to an

intrathecal dosage. The specific safe and effective amount will be vary, with such factors as the particular condition being treated, the administration route, the physical condition of the patient, the duration of treatment , the nature of the concurrent therapy (if any), the specific dosage form to be used, the carrier employed, the solubility of the formula therein and the dosage regimen desired for the composition. The dosage of 7.5 mg/week from Drug Facts and Comparisons could readily be converted to fit the instant claim limitation when an animal weighing 7.5 kg is treated (1mg/kg x 7.5 kg = 7.5 mg). Applicant's arguments with the encompassed calculations are based on a "human" while the instant claims are drawn to treatment of an "animal".

Applicant states that the '716 patent teaches that the problems associated with administration of drugs by routes such as intrathecal administration can be ameliorated by administering the drug in the form of a complex between the drug and a cyclodextrin. Applicant further asserts that "nowhere does the patent teach or suggest that it is advisable to do so without first complexing drugs using their invention". In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The '716 reference states that "methotrexate is commonly used intrathecally to obtain high neuraxial concentration". In this recitation there is no mention of cyclodextrin complexation. The reference goes on to suggest that complexation of methotrexate

with cyclodextrin **may** favorably alter the redistribution kinetics after intrathecal or neuraxial administration (column 9, lines 1-8).

In holding an invention obvious in view of a combination of references, there must be some suggestion, motivation or teaching in the prior art that would have led a person of ordinary skill in the art to select the references and combine them in the way that would produce the claimed invention. This motivation may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. Here, filtered through the problem to be solved, the prior art disclosed that radiculopathy is frequently a concurrent symptom of rheumatoid arthritis, and that this problem can be addressed by employing methotrexate. In addition, by the time of the claimed invention, intrathecal administration of methotrexate was a well known route of administration. Accordingly, there was clear motivation to treat radiculopathy with intrathecal methotrexate.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./

Examiner
Art Unit 1614

June 15, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614